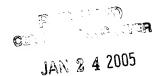
U.S.S.N. 09/978,333 Filed: October 15, 2001 AMENDMENT AND RESPONSE TO OFFICE ACTION



Amendment

In the Claims

- 1-6. (canceled)
- 7. (twice amended) A method for targeted recombination of a nucleic acid molecule comprising the steps of:
- a) providing a single stranded single-stranded oligonucleotide having a sequence that forms a triple stranded triple-stranded nucleic acid molecule that hybridizes by hybridizing with a target sequence double stranded in a double-stranded nucleic acid molecule and with a Kd of less than or equal to $2 \times 10^{-6} \cdot 10^{-7}$; and
- b) providing a donor nucleic acid such that recombination of the donor nucleic acid which recombines into the target sequence, is induced by triple helix formation between the single stranded single-stranded oligonucleotide and double stranded the double-stranded nucleic acid molecule.
- 8. (currently amended) The method of claim 7, wherein the single stranded singlestranded oligonucleotide is between 10 and 60 nucleotides in length.
- 9. (currently amended) The method of claim 7, wherein the single stranded singlestranded oligonucleotide is tethered to the donor DNA fragment nucleic acid.
- 10. (currently amended) The method of claim 7 wherein the double stranded doublestranded nucleic acid molecule encodes a protein and the targeted recombination of the donor nucleic acid with the double-stranded nucleic acid molecule alters the activity of the protein encoded by the double-stranded nucleic acid molecule.

450\$1925Vl

2

VII 132 079245/00045 U.S.S.N. 09/978,333 Filed: October 15, 2001

AMENDMENT AND RESPONSE TO OFFICE ACTION

- 11. (original) The method of claim 7, wherein the double-stranded nucleic acid molecule is selected from the group consisting of a gene, an oncogene, a defective gene, a viral genome, and a portion of a viral genome.
- 12. (currently amended) The method of claim 7, wherein the donor fragment nucleic acid is at least 30 nucleotide residues in length.
 - 13-14. (canceled)
- 15. (twice amended) The method of claim 7 to produce heritable changes in the genome of an intact human or animal further comprising the steps of:

injecting an administering the single-stranded oligonucleotide into an intact human or animal having a sequence that forms a triple-stranded nucleic acid molecule with a the target region sequence of located in the genome of the intact human or animal, and having a Kd of less than 2 x 10-6, wherein the the oligonucleotide binds to the target region sequence with a Kd of less than or equal to 2×10^{-7} , and mutates the target region sequence.

- 16. (original) The method of claim 15 wherein the oligonucleotide is between 10 and 60 nucleotides in length.
- 17. (original) The method of claim 15 wherein the oligonucleotide is dissolved in a physiologically acceptable carrier.
 - 18. (original) The method of claim 15 wherein the oligonucleotide is recombinagenic.
- 19. (currently amended) The method of claim 18 wherein the oligonucleotide stimulates recombination of an exogenously supplied DNA fragment donor nucleic acid with the target region sequence of the genome.

45051925VI

3

YU 132 078245/00045 U.S.S.N. 09/978,333 Filed: October 15, 2001

AMENDMENT AND RESPONSE TO OFFICE ACTION

- 20. (currently amended) The method of claim 18 wherein the oligonucleotide stimulates recombination of a tethered DNA fragment donor nucleic acid that is tethered to the oligonucleotide with the target region sequence of the genome.
- 21. (currently amended) The method of claim 15 wherein the target region sequence is selected from the group consisting of a gene, an oncogene, a defective gene, a viral genome, and a portion of a viral genome.
- 22. (currently amended) The method of claim 21 wherein the gene is a defective hemoglobin gene, cystic fibrosis gene, xerderma xeroderma pigmentosum gene, nucleotide excision repair pathway gene, or hemophilia gene.
- 23. (original) The method of claim 15 wherein the oligonucleotide is composed of homopurine or homopyrimidine nucleotides.
- 24. (previously presented) The method of claim 15 wherein the oligonucleotide is composed of polypurine or polypyrimidine nucleotides.
- 25. (currently amended) The method of claim 9 wherein the donor fragment nucleic acid is between 10 and 40 nucleotides.

4

YU 132 07874\$/00045